

Amendments to the Specification

Please replace the paragraphs beginning at page 17, line 6, with the following rewritten paragraphs:

There is no limit as to the length of the peptide linkers that can be used in the present invention. The length can be appropriately selected by those skilled in the art according to purpose. The length of a peptide linker for an scFV is typically one to 100 amino acids, preferably five to 30 amino acids, and particularly preferably 12 to 18 amino acids (for example, 15 amino acids). Examples of the amino acid sequences of such peptide linkers of the present invention include:

Ser

Gly•Ser

Gly•Gly•Ser

Ser•Gly•Gly

Gly•Gly•Gly•Ser (SEQ ID NO: 43)

Ser•Gly•Gly•Gly (SEQ ID NO: 44)

Gly•Gly•Gly•Gly•Ser (SEQ ID NO: 45)

Ser•Gly•Gly•Gly•Gly (SEQ ID NO: 46)

Gly•Gly•Gly•Gly•Gly•Ser (SEQ ID NO: 47)

Ser•Gly•Gly•Gly•Gly•Gly (SEQ ID NO: 48)

Gly•Gly•Gly•Gly•Gly•Gly•Ser (SEQ ID NO: 49)

Ser•Gly•Gly•Gly•Gly•Gly•Gly (SEQ ID NO: 50)

(Gly•Gly•Gly•Gly•Ser (SEQ ID NO: 51))_n

(Ser•Gly•Gly•Gly•Gly (SEQ ID NO: 52))_n

Ala•Ala•Asp•Ala•Ala•Ala•Ala•Gly•Gly•Pro•Gly•Ser (SEQ ID NO: 53)

where n is an integer of one or more.

Please replace the paragraph beginning at page 29, line 7, with the following rewritten paragraph:

Aqueous solutions for injection include, for example, physiological saline and isotonic solutions containing dextrose or other adjuvants (for example, D-sorbitol, D-mannose, D-mannitol, and sodium chloride). Appropriate solubilizers, for example, alcohols (ethanol and such), polyalcohols (propylene glycol, polyethylene glycol, and such), non-ionic detergents (~~polysorbate 80~~TM Polysorbate 80TM, HCO-50, and such), may be used in combination.

Please replace the paragraph beginning at page 31, line 30, with the following rewritten paragraph:

40 pmol each of the synthetic DNAs was added to each of the tubes. 25 µl of reaction solution that contained a dNTP mix comprising dATP, dGTP, dTTP, and dCTP (250 µM each), 1x TaKaRa ~~pyrobest~~TM PyrobestTM DNA Polymerase buffer, and 1.25 units of TaKaRa ~~pyrobest~~TM PyrobestTM DNA Polymerase was prepared in each tube. The tubes were placed in a thermal cycler Gene Amp PCR System 2400 (Perkin Elmer)(this thermal cycler was used for all reactions described herein below). The thermal cycling was carried out under the following condition: denaturation at 94°C for one minute, followed by five cycles of 94°C for 30 seconds and 72°C for 30 seconds. The second assembly step used the following four tubes:

- (1) tube 1: the reaction product of tube A and B,
- (2) tube 2: the reaction product of tube B and C,
- (3) tube 3: the reaction product of tube D and E, and
- (4) tube 4: the reaction product of tube E and F.

Please replace the paragraphs beginning at page 32, line 15, with the following rewritten paragraphs:

PCR was carried out after the three assembly steps described above. This PCR used two tubes. The first tube (tube H) contained 50 µl of reaction solution containing 1 µl of the reaction product of tube 1+2, 40 pmol each of the outer primers KMTR1 H1 (SEQ ID NO: 26) and KMTR1 H2 (SEQ ID NO: 27), a dNTP mix comprising dATP, dGTP, dTTP, and dCTP (250 µM each), 1x TaKaRa ~~pyrobest~~TM PyrobestTM DNA Polymerase buffer, and 2.5 units of TaKaRa ~~pyrobest~~TM PyrobestTM DNA Polymerase. The other tube (tube L) contained 50 µl of reaction solution containing 1 µl of the reaction product of tube 3+4, 40 pmol each of the outer primers KMTR1 L1 (SEQ ID NO: 28) and KMTR1 L2 (SEQ ID NO: 29), a dNTP mix comprising

dATP, dGTP, dTTP, and dCTP (250 μ M each), 1x TaKaRa ~~pyrobest~~TM-PyrobestTM DNA Polymerase buffer, and 2.5 units of TaKaRa ~~pyrobest~~TM-PyrobestTM DNA Polymerase. The samples in tubes H and L were denatured in the thermal cycler for one minute at 94°C, then 30 cycles of 94°C for 30 seconds and 72°C for 30 seconds were carried out.

Each of the products obtained by the PCR described above were further assembled and amplified by PCR as follows: First, 2.5 μ l each of the products obtained in tubes H and L was added to a single tube K, and 50 μ l of reaction solution was prepared, containing a dNTP mix comprising dATP, dGTP, dTTP, and dCTP (250 μ M each), 1x TaKaRa ~~pyrobest~~TM-PyrobestTM DNA Polymerase buffer, and 2.5 units of TaKaRa ~~pyrobest~~TM-PyrobestTM DNA Polymerase. After denaturation in the thermal cycler at 94°C for one minute, five cycles of 94°C for 30 seconds and 72°C for 30 seconds were carried out. Then, 1 μ l of the reaction product obtained in tube K was added to tube K-2. The prepared tube K-2 contained 50 μ l of reaction solution containing 40 pmol each of the outer primers KMTR1 H1 (SEQ ID NO: 26) and KMTR1 L2 (SEQ ID NO: 29), a dNTP mix comprising dATP, dGTP, dTTP, and dCTP (250 μ M each), 1x TaKaRa ~~pyrobest~~TM-PyrobestTM DNA Polymerase buffer, and five units of TaKaRa ~~pyrobest~~TM-PyrobestTM DNA Polymerase. After denaturation in the thermal cycler at 94°C for one minute, 30 cycles of 94°C for 30 seconds and 72°C for 60 seconds were carried out. The reaction products were separated on a 1.2% agarose gel by electrophoresis, and a fragment with a target size of 800 bp was extracted from the gel and purified using a QIAquick Gel Extraction Kit (QIAGEN). Then, the fragment was digested using the restriction enzymes *Eco*RI and *Not*I, and purified using a QIAquick Nucleotide Removal Kit (QIAGEN). The resulting fragment was inserted into the expression vector pCXND3 pretreated with the restriction enzymes *Eco*RI and *Not*I, and the nucleotide sequence was determined. The plasmid comprising the target sequence was named pCXND3/KMTR1#33.

Please replace the paragraphs beginning at page 33, line 30, with the following rewritten paragraph:

In tube 2-1, 50 pmol each of the primers KMTR1 H1 and ScFv2A was added to the following reaction solution (hereinafter in Sections 1-2, 1-3-2, and 1-4-2, this is referred to as the "PCR reaction solution"): 50 μ l (final volume) of reaction solution containing 100 ng of pCXND3/KMTR1#33 as a template, a dNTP mix comprising dATP, dGTP, dTTP, and dCTP (250 μ M each), 1x TaKaRa ~~pyrobest~~TM-PyrobestTM DNA Polymerase buffer, and five units of

TaKaRa-pyrobTMest PyrobTMest DNA Polymerase. After tube 2-1, which contained this PCR reaction solution, was denatured in the thermal cycler at 94°C for one minute, 30 cycles of 94°C for 30 seconds and 72°C for 60 seconds were carried out. The reaction products were separated on a 1.2% agarose gel by electrophoresis, and a fragment with a target size of 400 bp was extracted from the gel and purified using a QIAquick Gel Extraction Kit (QIAGEN).

Please replace the paragraphs beginning at page 34, line 10, with the following rewritten paragraph:

1 µl each of the DNA fragments obtained in tube 2-1 and tube 2-2 was added to the reaction solution described below (in section 1-2 shown below, referred to as the “assembly solution”): 50 µl (final volume) of reaction solution containing a dNTP mix comprising dATP, dGTP, dTTP, and dCTP (250 µM each), 1x TaKaRa pyrobTMest-PyrobTMest DNA Polymerase buffer, and five units of TaKaRa pyrobTMest-PyrobTMest DNA Polymerase. After the solution in Tube 2 was denatured in the thermal cycler at 94°C for one minute, the DNAs were assembled by five cycles of 94°C for 30 seconds and 72°C for 60 seconds. Then, 0.5 µl each of 100 µM KMTR1 H1 and KMTR1 L2 was added to the reaction solution. After denaturation at 94°C for one minute, the DNA was amplified by 30 cycles of 94°C for 60 seconds and 72°C for 60 seconds. The reaction products were separated on a 1.2% agarose gel by electrophoresis, and a fragment with a target size of 800 bp was extracted from the gel and purified using a QIAquick Gel Extraction Kit (QIAGEN). The purified fragment was digested with the restriction enzymes *EcoRI* and *NotI*, and inserted into the expression vector pCXND3, which had been pre-cleaved with the restriction enzymes *EcoRI* and *NotI*. The nucleotide sequence of the fragment was determined. The plasmid comprising the target sequence was named pCXND3/KMTR1ScFv2.

Please replace the previous sequence listing with the enclosed sequence listing.